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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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TIMOTHY R SCHWARTZ PH D
GENENTECH INC
1 DNA WAY
SOUTH SAN FRANCISCO CA 94080-4990

EXAMINER	
FORMAN, B	

ART UNIT	PAPER NUMBER
1655	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	09/449,204	SINICROPI ET AL.	
	Examiner	Art Unit	
	BJ Forman	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on *21 October 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. This action is in response to papers filed 10 October 2000 in Paper No. 10 in which claims 1, 10, 15, 16, 22 and 23 were amended and claim 21 was canceled. All of the amendments have been thoroughly reviewed and entered. The substitute Specification is acknowledge and entered. The previous rejections stated in the Office Action of Paper No. 7 dated 30 June 2000 under 35 U.S.C. 112, second paragraph are withdrawn in view of the amendments. The previous rejections stated in Paper No. 7 under 35 U.S.C. 103(a) are maintained. All of the arguments have been thoroughly reviewed and are discussed below.

Currently claims 1-20 and 22-23 are under prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-5, 7-12, 15, 16 & 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hendrickson et al. (Nucleic Acids Research, 1995, 23(3): 522-529) in view of Gibson et al. (Genome Methods 1996, 6: 995-1001).

Regarding Claim 1, Hendrickson et al. teach a method for quantitating or detecting the presence of a target compound in a sample which may contain the target compound, the method comprising: exposing the sample to a capture molecule which binds to the target molecule to form a capture molecule-target molecule complex, adding to the complex a nucleic acid moiety containing a detector molecule wherein the detector molecule binds to the target molecule to form a capture molecule-target molecule-detector molecule complex, amplifying the

nucleic acid moiety by PCR amplification, and quantitating or detecting the PCR amplified nucleic acid moiety (page 523, Fig. 1). Hendrickson et al. teach the amplified nucleic acid moiety is quantitated and detected on an agarose gel by detection of moiety-specific size. Hendrickson et al. do not teach the amplified nucleic acid moiety is quantitated or detected by a detectable non-primer probe. However, detectable non-primer probes were known and routinely practiced in the art for the detection of PCR products at the time the claimed invention was made as taught by Gibson et al. (page 1000, Table 1). Specifically, Gibson et al. teach a method for detecting the presence of a target compound wherein the target compound is PCR amplified and detected with sequence-specific non-primer probes (page 1000, last paragraph and Table 1). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Hendrickson et al. with the teachings of Gibson et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the size-specific detection and quantitation of Hendrickson et al. with the sequence-specific non-primer probe detection of Gibson et al. for the obvious benefit of eliminating the agarose gel step.

Regarding Claim 2, Hendrickson et al. teach the method of Claim 1 further comprising washing the capture molecule-target molecule complex to remove unbound sample after step (a) (page 525, left column, third full paragraph, lines 5-6).

Regarding Claim 3, Hendrickson et al. teach the method of Claim 1 further comprising washing the capture molecule-target molecule complex to remove unbound sample after step (b) (page 525, left column, third full paragraph, lines 11-13).

Regarding Claim 4, Hendrickson et al. teach the method of Claim 1 wherein the capture molecule is bound to a solid support (page 1372, Fig. 1).

Regarding Claim 5, Hendrickson et al. teach the method of Claim 1 wherein the capture molecule is bound to a solid support (page 1372, Fig. 1) but they do not teach the method wherein the capture molecule is in solution during step (a) or (b). However, binding of capture

molecule-target molecules in solution was routinely practiced in the art. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Hendrickson et al. with routinely practiced protocols to obtain the claimed invention because one skilled in the art would have been motivated with a reasonable expectation of success to modify the method of Hendrickson et al. wherein the capture molecules are immobilized with capture molecules in solution for the known benefit of binding capture-to-target molecules in large volumes for the obvious benefit of more rapid binding in solution as known in the art.

Regarding Claim 7, Hendrickson et al. teach the method of Claim 1 wherein the capture molecule is a DNA labeled antibody and the detector molecule is a DNA labeled antibody (page 523, Fig. 1) but they do not teach the capture molecule is a DNA labeled antibody. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the time the claimed invention was made to simplify the method of Hendrickson et al. to obtain the claimed invention because one skilled in the art would have been motivated with a reasonable expectation of success to label the capture molecule for single molecule capture and detection for the obvious benefit of eliminating the labeled detector molecule.

Regarding Claim 8, Hendrickson et al. teach the method of Claim 1 wherein the target molecule is an organic compound having a molecular weight of about 100 to about 1000 grams/mole i.e. human thyroid stimulating hormone (hTSH) (page 523, left column, second full paragraph, lines 1-3).

Regarding Claim 9, Hendrickson et al. teach the method of Claim 1 wherein the target molecule is a protein i.e. hTSH (page 523, left column, second full paragraph, lines 1-3).

Regarding Claim 10, Hendrickson et al. teach the method of Claim 1 wherein the target molecule is a protein i.e. hTSH (page 523, left column, second full paragraph, lines 1-3).

Regarding Claim 11, Hendrickson et al. do not teach the method wherein the sample is selected from the group consisting of blood, serum, sputum, urine, semen, cerebrospinal fluid,

bronchial aspirate and organ tissue. However, Hendrickson et al. teach the method detects hTSH and therefore has utility in the detection of hTSH which is known to be present in blood (page 526, left column, last paragraph). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Hendrickson et al. with the teachings of Hendrickson et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to apply the method of Hendrickson et al. for the expected benefit of highly sensitive detection of a target molecule in blood as taught by Hendrickson et al. (page 528, last paragraph).

Regarding Claim 12, Hendrickson teach the method of Claim 1 wherein the capture molecule is immobilized on a solid support (page 525, left column, second full paragraph, lines 1-6) but they do not teach the immobilization is via biotin labeled capture molecule bound to a streptavidin or avidin labeled support. However, biotin-labeled capture molecules immobilized via binding to a streptavidin or avidin labeled support were known and routinely practiced in the art at the time the claimed invention was made. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Hendrickson et al. with routinely practiced procedures to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the immobilization of Hendrickson et al. and to immobilize the capture molecule by biotin-avidin interaction for the known benefit of rapid and specific biotin-avidin binding.

Regarding Claim 15, Hendrickson et al. teach the method of Claim 1 wherein the target molecule is quantitated at a concentration of $\leq 10^{-12}$ grams/mL (page 527, first paragraph and Fig. 5).

Regarding Claim 16, Hendrickson et al. teach the method of Claim 1 wherein the target molecule is quantitated at a concentration of about 10^{-8} grams/mL to about 10^{-15} grams/mL (page 527, first paragraph and Fig. 5).

Regarding Claim 20, Hendrickson et al. teach the method of Claim 1 wherein the solid support is a 96-well thermowell microtitre plate which is placed into a thermal cycler for PCR amplification (page 525, left column, second full paragraph, lines 1-4 and fourth paragraph, lines 1-3) but they do not teach the solid support is a PCR tube. However, 96-well microtitre plates and PCR tubes were known and routinely practiced in the art for one-well/sample and one-tube/sample wherein reagent mixing and nucleic acid amplification for each sample is in isolation. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Hendrickson et al. with routine practiced procedures to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the solid support of Hendrickson et al. wherein the solid support provides 96-wells for 96 samples based the number of samples to be assayed, available equipment and experimental design for the obvious benefit of reducing the labor and cost of 96-format assays.

4. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hendrickson et al. (Nucleic Acids Research, 1995, 23(3): 522-529) in view of Gibson et al. (Genome Methods 1996, 6: 995-1001) as applied to claim 1 above, and further in view of Kawazoe et al. (Biotechnology Progress, 1997, 13: 873-874). Hendrickson et al. teach a method for quantitating or detecting the presence of a target compound in a sample, the method comprising: exposing the sample to a capture molecule which binds to the target molecule for capture molecule-target molecule binding to form a capture molecule-target molecule complex (page 523, Fig. 1), wherein the capture molecule is an antibody (page 525, left column, second

full paragraph, lines 1-3). Hendrickson et al. do not teach the capture molecule is an aptamer. However, aptamers were known in the art and routinely used as capture molecules to form capture molecule-target molecule complexes as taught by Kawazoe et al. Specifically, Kawazoe et al teach a method to detect a target molecule in a sample wherein a capture molecule, which is an aptamer, binds the target molecule to form a capture molecule-target molecule complex for detection and quantitation of the target molecule (page 873, right column, last paragraph). Additionally, Kawazoe et al. teach the advantages of aptamers over antibodies as capture molecules i.e. because they are not produced by organisms which requires cell culture purification, they can be synthesized rapidly, reproducibly and accurately by automated processes,(page 873, left column, second paragraph). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Hendrickson et al. with the teachings of Kawazoe et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the antibody capture molecule of Hendrickson et al. with the aptamer capture molecules of Kawazoe et al. in view of the advantages taught by the latter reference.

5. Claims 13 & 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hendrickson et al. (Nucleic Acids Research, 1995, 23(3): 522-529) in view of Gibson et al. (Genome Methods 1996, 6: 995-1001) as applied to claim 1 above. Hendrickson et al. teach a method for quantitating or detecting the presence of a target compound, the method comprising: exposing the sample to a capture molecule to form a capture molecule-target molecule complex, adding to the complex a nucleic acid moiety containing a detector molecule and amplifying the nucleic acid moiety by PCR amplification (page 523, Fig. 1) wherein the amplified nucleic acid moiety is quantitated or detected on an agarose gel (page 525, right column, second full paragraph).

Regarding Claim 13, Hendrickson et al. do not teach quantitation or detection using a non-primer probe having a fluorescent dye label. However, Gibson et al. teach quantitation of the amplified nucleic acid moiety using a detectable non-primer probe having a fluorescent dye label (page 996, right column lines 1-4).

Regarding Claim 14, Gibson et al. teach the method wherein the fluorescent dye label comprises two dyes, a reporter dye and a quencher dye which fluoresce at different wavelengths (page 996, right column lines 1-16).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Hendrickson et al. with the teachings of Gibson et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the detection of Hendrickson et al. with the Gibson et al. method wherein the PCR reaction is detected and quantitated by fluorescently labeled non-primer probes by monitoring fluorescence emission and quenching (page 996, right column, lines 1-16) for the obvious benefit of detecting and quantitating amplified product over an extended period of time and for the expected benefit of accurate and time-saving detection as taught by Gibson et al. (page 995, right column, lines 1-5).

6. Claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hendrickson et al. (Nucleic Acids Research, 1995, 23(3): 522-529) in view of Gibson et al. (Genome Methods 1996, 6: 995-1001) as applied to claim 1 above and further in view of Gold et al. (U.S. Patent No. 5,475,096, filed 10 June 1991). Hendrickson et al. teach a method for quantitating or detecting the presence of a target compound, the method comprising: exposing the sample to a capture molecule to form a capture molecule-target molecule complex, adding to the complex a nucleic acid moiety containing a detector molecule and amplifying the nucleic

acid moiety by PCR amplification (page 523, Fig. 1) wherein the nucleic acid moiety is DNA (page 523, right column, last paragraph and Fig. 2).

Regarding Claim 17, Hendrickson et al. do not teach the detector molecule is RNA and the RNA is reverse transcribed to form DNA before or during amplifying. However, Gold et al. teach a method for detecting the presence of a target molecule wherein the detector molecule is RNA and is reverse transcribed to form DNA before PCR amplification (Column 9, lines 14-40)

Regarding Claim 18, Gold et al. teach the RNA is reverse transcribed at a temperature sufficient to dissociate the detector molecule from the capture molecule-target molecule-detector molecule complex and reverse transcribed (Example 1, Column 36, lines 58-61).

Regarding Claim 19, Gibson et al. teach the RNA is dissociated from the complex and reverse transcribed under conditions known in the art (Example 1, Column 36, lines 62-67).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Hendrickson et al. with the teachings of Gold et al. and Gibson et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the detector molecule of Hendrickson et al. with the RNA detector molecule of Gold et al. for the expected benefit of identifying nucleic acid ligands as taught by Gold et al. (Column 1, lines 14-31).

7. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hendrickson et al. (Nucleic Acids Research, 1995, 23(3): 522-529) in view of Gibson et al. (Genome Methods 1996, 6: 995-1001). Hendrickson et al. teach a method for quantitating or detecting the presence of a target compound in a sample which may contain the target compound, the method comprising: exposing the sample to a capture antibody which binds to the target molecule to form a capture molecule-target molecule complex, adding to the complex a nucleic acid moiety containing a detector molecule wherein the detector molecule binds to the target

molecule to form a capture molecule-target molecule-detector molecule complex, amplifying the nucleic acid moiety by PCR amplification, and quantitating or detecting the PCR amplified nucleic acid moiety (page 523, Fig. 1). Hendrickson et al. do not teach the method wherein the amplified nucleic acid is quantitated or detected using a detectable non-primer probe and real-time PCR. However, real-time PCR and detectable non-primer probes were known and routinely practiced in the art at the time the claimed invention was made as taught by Gibson et al. Specifically, Gibson et al. teach a method for detecting a PCR amplified product with sequence-specific non-primer probes using real-time PCR (page 997, right column, page 1000, last paragraph and Table 1). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Hendrickson et al. with the teachings of Gibson et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the detection of Hendrickson et al. wherein aliquots of the PCR reaction are run on agarose gel for detection and quantitation of amplified product at one time point (page 525, right column, second full paragraph) with the Gibson et al. method wherein the PCR reaction is detected and quantitated every 8.5 seconds (page 996, left column, lines 1-3) by detection of non-primer probe hybridization for the obvious benefit of eliminating the agarose gel step and of detecting and quantitating over an extended period of time and for the expected benefit of accurate and time-saving detection as taught by Gibson et al. (page 995, right column, lines 1-5). The skilled practitioner would have been further motivated to use a biotinylated aptamer and immobilize the biotinylated ternary complex with streptavidin for the known benefit of rapid isolations as routinely practiced in the art.

8. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hendrickson et al. (Nucleic Acids Research, 1995, 23(3): 522-529) in view of Gibson et al. (Genome Methods

1996, 6: 995-1001) and Kawazoe et al. (Biotechnology Progress, 1997, 13: 873-874). Hendrickson et al. teach a method for quantitating or detecting the presence of a target compound in a sample, the method comprising: exposing the sample to a capture molecule which binds to the target molecule to form a capture molecule-target molecule complex, adding to the complex a nucleic acid moiety containing a detector molecule wherein the detector molecule binds to the target molecule to form a capture molecule-target molecule-detector molecule complex, amplifying the nucleic acid moiety by PCR amplification, and quantitating or detecting the PCR amplified nucleic acid moiety (page 523, Fig. 1). Hendrickson et al. do not teach the method wherein the detector molecule is an RNA aptamer and the amplified RNA is quantitated or detected using a detectable non-primer probe and real-time PCR. However, aptamers were known in the art as taught by Kawazoe et al. and real-time PCR and detectable non-primer probes were known and routinely practiced in the art at the time the claimed invention was made as taught by Gibson et al. Specifically, Gibson et al. teach a method for detecting a PCR amplified product with sequence-specific non-primer probes using real-time PCR (page 997, right column, page 1000, last paragraph and Table 1). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Hendrickson et al. with the teachings of Gibson et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the detection of Hendrickson et al. wherein aliquots of the PCR reaction are run on agarose gel for detection and quantitation of amplified product at one time point (page 525, right column, second full paragraph) with the Gibson et al. method wherein the PCR reaction is detected and quantitated every 8.5 seconds (page 996, left column, lines 1-3) by detection of non-primer probe hybridization for the obvious benefit of eliminating the agarose gel step and of detecting and quantitating over an extended period of time and for the expected benefit of accurate and time-saving detection as taught by Gibson et al. (page 995, right column, lines 1-5). Additionally, it would have been *prima facie* obvious to

one skilled in the art at the time the claimed invention was made to modify the method of Hendrickson et al. with the teaching of Kawazoe et al. to obtain the claimed invention because one skilled in the art would have been motivated with a reasonable expectation of success to modify the detector molecule of Hendrickson et al. wherein the detector molecule is an antibody containing a nucleic acid moiety with the teaching of Kawazoe et al. who teach the advantages of aptamers over antibodies i.e. because they are not produced by organisms which requires cell culture purification, they can be synthesized rapidly, reproducibly and accurately by automated processes,(page 873, left column, second paragraph) based the apatmer's functionality which comprises both the antibody detector molecule's binding and in view of the advantages taught by Kawazoe et al.

Response to Arguments

9. Applicant argues that one of ordinary skill in the art would not have been motivated to use the probe detection of Gibson et al in the detection method of Hendrickson et al. to eliminate the agarose gel step of Hendrickson et al. because the detection of Gibson et al. is limited and requires extra steps. Specifically, Applicant argues that because the Gibson et al. detection method limits concentrations of target and internal control RNA or DNA and uses more than one PCR tube which require extra steps, the method is not simpler and more efficient and one of skill in the art would not have been motivated to combine the teaching of Hendrickson et al. and Gibson et al. This argument is not found persuasive because one of ordinary skill in the art would have been motivated to apply the detection of Gibson et al. to the method of Hendrickson et al. for the expected benefit of simplicity i.e. the simplicity of a second PCR tube compared to an agarose gel which requires numerous extra steps of mixing, pouring, solidifying, sample preparation, sample loading, running and reading. Additionally, the argument is not found persuasive because the concentration limits and number of PCR tubes are not limitations in the claims.

Applicant argues that the references alone or in combination would not have been sufficient to suggest the present invention because Gibson is limited to quantitating mRNA and only 1000 copies of mRNA/tube can be measured. This argument is not found persuasive because Gibson et al. is not "limited" to mRNA, but uses mRNA in the initial step of RT-PCR to produce DNA for the subsequent PCR amplification (note: DNA polymerase and dNTPs, page 1000, right column last paragraph). Gibson also teaches as little as 1000 copies of mRNA per tube can be measured and results suggest as little as 500-copy detection (page 999, left

column, second full paragraph). Additionally, the arguments are not found persuasive because the claims do recite non-mRNA limitations and copy number limitations. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., non-mRNA and copy number) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that the examiner has impermissibly used hindsight reconstruction to achieve the present invention. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant further argues that Gibson et al. teaches away from the claimed invention because the use of fluorescent reporter dyes is limited due to overlapping spectra of know usable dyes. This argument is not found persuasive because the overlapping spectra problem only occurs when the target and control samples in the same tube and their concentration differs by less than 1000-fold (page 996, left column, first full paragraph, lines 12-14). The simplicity of more than one tube compared to detection on an agarose gel is discussed above.

10. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.

October 30, 2000

STEPHANIE W. LANGER
PRIMARY EXAMINER